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Experiment Design Based on Bayes Risk and Weighted Bayes Risk with Application to Pharmacokinetic Systems

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This report investigates an experimental design method, MMopt, which minimizes an overbound on the Bayes Risk. MMopt provides an advantageous alternative to D-optimality and other criteria based on the asymptotic Fisher Information matrix. Advantages of MMopt are: (1) it avoids the circular reasoning associated with having to know a patient's true parameters in order to design an experiment; (2) it avoids using an asymptotic information measure for an experiment design that only places a small number of samples; (3) it is optimized using time-response data only. This last property is very powerful, permitting optimization with or without a specific structural model.

A new result is presented that introduces weighting into the Bayes risk cost. The weighted form of MMopt is especially useful for PK problems, where the experiment design can be tailored to be most informative about specific metrics such as AUC, maximal concentration, or what best future dose to give. A theoretical result shows that the weighted MMopt preserves the overbound of [1]. This is important because it allows bound-optimal designs to be systematically calculated as in the unweighted MMopt case. MMopt appears superior to ED optimal design, which also incorporates a Bayesian prior, when applied to several problems of practical interest.

[1] Blackmore L, Rajamanoharan S, and Williams BC, "Active Estimation for Jump Markov Linear Systems," IEEE Trans. Automatic Control., Vol. 53, No. 10., pp. 2223-2236, Nov. 2008.

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